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L11: Entry 9 of 39

File: USPT

Apr 30, 2002

DOCUMENT-IDENTIFIER: US 6380259 B2

TITLE: Use of substituted amidino compounds in the treatment of chronic obstructive pulmonary disease

Brief Summary Text (154):

The maleate (2-butenedioate) salt of the compound of formula IB in which R.sub.1 is di-isopropylamino, R.sub.2 is hydroxy, R.sub.3 is hydrogen, X.sub.1 and X.sub.3 are --O-- and X.sub.2 is pentylene is novel per se. This salt, 4-[5-[4-(aminoiminomethyl)phenoxy]pentoxy]-2-hydroxy-N,N-bis(1-methylethyl )benzamide (Z)-2-butenedioate may be prepared as described in the Example hereinafter.

Brief Summary Text (162):

Preferred compositions for enteral or parenteral administration are tablets and gelatin capsules comprising the active ingredient together with a) diluents, e.g. lactose, dextrose, sucrose, mannitol, sorbitol, cellulose and/or glycine; b) lubricants, e.g. silica, talcum, stearic acid, its magnesium or calcium salt and/or polyethyleneglycol; for tablets also c) binders e.g. magnesium aluminum silicate, starch paste, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose and or polyvinylpyrrolidone; if desired d) disintegrants, e.g. starches, agar, alginic acid or its sodium salt, or effervescent mixtures; and/or e) absorbants, colorants, flavors and sweeteners. Injectable compositions are preferably aqueous isotonic solutions or suspensions, and suppositories are advantageously prepared from fatty emulsions or suspensions. Said compositions may be sterilized and/or contain adjuvants, such as preserving, stabilizing, wetting or emulsifying agents, solution promoters, salts for regulating the osmotic pressure and/or buffers. Cores of coated tablets are provided with suitable, optionally enteric, coatings, using, inter alia, concentrated sugar solutions which optionally contain gum arabic, talc, polyvinylpyrrolidone, polyethylene glycol and/or titanium dioxide, lacquer solutions in suitable organic solvents or solvent mixtures or, for the preparation of enteric coatings, solutions of suitable cellulose products such as acetyl cellulose phthalate or hydroxypropylmethylcellulose phthalate. Colorants or pigments can be added to the tablets or coatings of coated tablets, for example, to identify or to indicate various doses of active compound. In addition, they may also contain other therapeutically valuable substances. Said compositions are prepared according to conventional mixing, granulating or coating methods, respectively, and contain about 0.1 to 75%, preferably about 1 to 50%, of the active ingredient.

Detailed Description Text (2):

4-[5-[4-(amino(hydroxyimino)methyl)phenoxy]pentoxy]-2-hydroxy-N,N-bis(1-methylethyl)benzamide prepared as described in U.S. Pat. No. 5,455,274 (100.76 g), 370 mL of acetic acid, and 800 mL of ethanol are gently shaken and warmed to 50-52.degree. C. to form a slightly yellow solution. 10% palladium-carbon (13.2 g) is added and the mixture is hydrogenated at 60 psi at a temperature 52-54.degree. C. for 24 hours. The hot reaction mixture is filtered through a celite and the filter cake is washed twice with 75 mL of 2:1 ethanol/acetic acid. The solvents are then removed in vacuo at 75.degree. C. Toluene (200 mL) is added to the residue and the solvents are evaporated in vacuo. This is repeated a second time to remove trace amounts of acetic acid and ethanol. To the residue is added 10 g of activated charcoal and 50 mL of 2-propanol, and the mixture is heated to 75.degree. C. The

slurry is filtered hot and washed twice with 50 mL of 2-propanol. 4-[5-[4-(aminoiminomethyl)phenoxy]pentoxy]-2-hydroxy-N,N-bis(1-methylethyl )benzamide monoacetate is crystallized from 2-propanol as the product, m.p. 197-199.degree. C.

Detailed Description Text (3):

4-[5-[4-(aminoiminomethyl)phenoxy]pentoxy]-2-hydroxy-N,N-bis(1-methyleth yl)  
benzamide monoacetate (75.24 g) is suspended in 550 mL of anhydrous ethanol (550 mL) and stirred under a nitrogen atmosphere and heated to 75.degree. C. A solution of 34.82 g of maleic acid in 75 mL of water is heated to 75.degree. C. and rapidly added to the mixture. Then 7 g of activated carbon is added, and the black slurry is heated to 80.degree. C. and filtered through a celite layer. The filter-cake is washed with ethanol/water (85 ml/15 mL), and cooled overnight to room temperature. The reaction mixture is cooled to 3.about.5.degree. C. for 2 hours and 4-[5-[4-(aminoiminomethyl)phenoxy]pentoxy]-2-hydroxy-N,N-bis(1-methylethyl )benzamide (Z)-2-butenedioate (1:1) is collected as white crystals, m.p. 212.degree. C.

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L11: Entry 20 of 39

File: USPT

Oct 3, 1995

DOCUMENT-IDENTIFIER: US 5455274 A

TITLE: Hydroxyamidine derivatives

Brief Summary Text (81):

Illustrative of the invention, the compound of example 1,4-[5-[4-[amino(hydroxyimino)methyl]phenoxy]pentyloxy]-2-hydroxy-N,N-bis(1-methylethyl)benzamide inhibits LTB.sub.4 -induced PMN aggregation at an IC.sub.50 of about 10 nM in vitro. Said compound also causes inhibition of LTB.sub.4 -induced neutropenia in the rat when administered at a dose of about 0.5 mg./Kg p.o., as determined at four hours after administration.

Brief Summary Text (173):

The pharmacologically active compounds of the invention are useful in the manufacture of pharmaceutical compositions comprising an effective amount thereof in conjunction or admixture with excipients or carriers suitable for either enteral or parenteral application. Preferred are tablets and gelatin capsules comprising the active ingredient together with a) diluents, e.g. lactose, dextrose, sucrose, mannitol, sorbitol, cellulose and/or glycine; b) lubricants, e.g. silica, talcum, stearic acid, its magnesium or calcium salt and/or polyethyleneglycol; for tablets also c) binders e.g. magnesium aluminum silicate, starch paste, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose and or polyvinylpyrrolidone; if desired d) disintegrants, e.g. starches, agar, alginic acid or its sodium salt, or effervescent mixtures; and/or e) absorbants, colorants, flavors and sweeteners. Injectable compositions are preferably aqueous isotonic solutions or suspensions, and suppositories are advantageously prepared from fatty emulsions or suspensions. Said compositions may be sterilized and/or contain adjuvants, such as preserving, stabilizing, wetting or emulsifying agents, solution promoters, salts for regulating the osmotic pressure and/or buffers. Cores of coated tablets are provided with suitable, optionally enteric, coatings, using, inter alia, concentrated sugar solutions which optionally contain gum arabic, talc, polyvinylpyrrolidone, polyethylene glycol and/or titanium dioxide, lacquer solutions in suitable organic solvents or solvent mixtures or, for the preparation of enteric coatings, solutions of suitable cellulose products such as acetyl cellulose phthalate or hydroxypropylmethylcellulose phthalate. Colorants or pigments can be added to the tablets or coatings of coated tablets, for example, to identify or to indicate various doses of active compound. In addition, they may also contain other therapeutically valuable substances. Said compositions are prepared according to conventional mixing, granulating or coating methods, respectively, and contain about 0.1 to 75 %, preferably about 1 to 50 %, of the active ingredient.

Detailed Description Text (2):

A stirred solution of 2-acetoxy-4-[5-(4-cyanophenoxy)pentyloxy]-N,N-bis(1-methylethyl)benzamide (20 g, 42.9 mmol) in 20 mL of water and 350 mL of ethanol is treated with sodium hydroxide (3.43 g, 85.8 mmol) and hydroxylamine hydrochloride (5.97 g, 85.9 mmol). After refluxing overnight, the reaction is concentrated in vacuo. The resulting material is purified by chromatography on silica gel (500 g) with 65-100% ethyl acetate/hexane followed by 30% methanol/ethyl acetate as the eluent. After concentration in vacuo, the residue is recrystallized with methanol, ethyl acetate, and hexane to afford 4-[5-[4-[amino(hydroxyimino)methyl]phenoxy]

pentyloxy]-2-hydroxy-N,N-bis(1-methylethyl)benzamide as colorless crystals, mp=195.degree.-197.degree. C.;

Detailed Description Text (4):

The starting material, 2-acetoxy-4-[5-(4-cyanophenoxy)pentyloxy]-N,N-bis(1-methylethyl)benzamide, can be prepared, for example, as follows:

Detailed Description Text (7):

A stirred solution of 4-[5-(4-cyanophenoxy)pentyloxy]-2-hydroxy-benzoic acid (28 g, 82 mmol) in 300 mL of dichloromethane is treated with pyridine (13.3 mL, 164 mmol) and acetic anhydride (9.3 mL, 98.4 retool) and stirred at room temperature for 30 minutes. The reaction is concentrated in vacuo and the residue is partitioned between ethyl acetate and 1N hydrochloric acid. The organic phase is washed with 1N hydrochloric acid and brine, dried over sodium sulfate, and concentrated in vacuo. The resulting 2-acetoxy-4-[5-(4-cyanophenoxy)pentyloxy]-benzoic acid is then dissolved in 300 mL of dichloromethane and treated at 0.degree. C. with oxalyl chloride (8.6 mL, 98.4 mmol) and N,N-dimethylformamide (7.6 mL, 98.4 mmol). This solution is stirred at room temperature for 30 minutes and treated with 30 mL of diisopropylamine at 0.degree. C. After stirring at room temperature for 30 minutes, the reaction is filtered and the filtrate is concentrated in vacuo. The resulting material is partitioned between ethyl acetate and 1N hydrochloric acid. The organic phase is washed with brine, dried over sodium sulfate, and concentrated in vacuo to afford 2-acetoxy-4-[5-(4-cyanophenoxy)pentyloxy]-N,N-bis(1-methylethyl)benzamide.

Detailed Description Text (15):

(b) 4-[5-[4-[amino(hydroxyimino)methyl]phenoxy]pentyloxy]-2-[(N-hydroxycarbamo yl)methoxy]-N,N-bis(1-methylethyl)benzamide as a colorless foam;

Detailed Description Text (18):

A stirred solution of 4-[5-(4-cyanophenoxy)pentyloxy]-2-hydroxy-N,N-bis(1-methylethyl)benzamide (1.0 g, 2.36 mmol) in 10.0 mL of N,N-dimethylformamide is treated with 60% sodium hydride (100 mg, 2.59 mmol) and ethyl bromoacetate (290 .mu.L, 2.59 mmol), and the mixture is heated at 70.degree. C. overnight; the reaction is partitioned between ethyl acetate and water, dried over sodium sulfate and concentrated in vacuo to afford a yellow foam. This material is purified by chromatography on silica gel (30 g) with 40-50% ethyl acetate/hexane as the eluent to afford ethyl 5-[5-(4-cyanophenoxy)pentyloxy]-2-[N,N-bis(1-methylethyl)aminocarbonyl]phenoxyacetate as a colorless foam.

Detailed Description Text (23):

A stirred solution of 2-acetoxy-4-[5-(4-cyanophenoxy)pentyloxy]-N,N-bis(1-methylethyl)benzamide (10 g, 21.5 mmol) in 250 mL of ethanol is treated with 1N sodium hydroxide solution (25 mL, 25 mmol). After stirring at room temperature for 2 hours, the reaction is concentrated in vacuo. This material is partitioned between ethyl acetate and 1N hydrochloric acid. The organic phase is washed with brine, dried over sodium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (200 g) with 40-50% ethyl acetate/hexane as the eluent to afford 4-[5-(4-cyanophenoxy)pentyloxy]-2-hydroxy-N,N-bis(1-methylethyl)benzamide as a colorless foam.

Detailed Description Text (24):

A stirred solution of 4-[5-(4-cyanophenoxy)pentyloxy]-2-hydroxy-N,N-bis(1-methylethyl)benzamide (5.7 g, 13.4 mmol) in 50 mL of acetone is treated with sodium hydroxide (5.4 g, 134 mmol) and heated to reflux. The reaction is treated slowly with chloroform (1.4 mL, 17.4 mmol) in 150 mL of acetone and refluxed for 4 hours. The reaction is concentrated in vacuo and the residue is partitioned between ethyl acetate and 1N hydrochloric acid. The organic phase is washed with brine, dried over magnesium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (200 g) with 0-10% methanol/ethyl acetate as the eluent to afford 2-[5-[5-(4-cyanophenoxy)pentyloxy]-2-[N,N-bis(1-

methylethyl)aminocarbonyl]phenoxy]-2-methylpropanoic acid as a colorless foam.

Detailed Description Text (30):

A stirred solution of 4-[5-(4-cyanophenoxy)-pentyloxy]-N,N-bis(1-methylethyl)benzamide (300 mg, 0.73 mmol) in 2 mL of water and 8 mL of ethanol is treated with sodium hydroxide (32 mg, 0.81 mmol) and hydroxylamine hydrochloride (56 mg, 0.81 mmol). After refluxing overnight, the reaction is partitioned between dichloromethane and brine. The organic phase is dried over sodium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (10 g) with 70-80% ethyl acetate/hexane as the eluent to afford 4-[5-[4-[amino(hydroxyimino)methyl]phenoxy]pentyloxy]-N,N-bis-(1-methylethyl)benzamide as colorless crystals, m.p.=146.degree.-149.degree. C.;

Detailed Description Text (32):

The starting material, 4-[5-(4-cyanophenoxy)pentyloxy]-N,N-bis(1-methylethyl)benzamide, can be prepared, for example, as follows:

Detailed Description Text (33):

A stirred solution of 4-hydroxybenzoic acid (5 g, 36.2 mmol) in 50 mL of dichloromethane is treated at 0.degree. C. with oxalyl chloride (6.3 mL, 72.4 mmol) and N,N-dimethylformamide (5.6 mL, 72.4 mmol). This solution is stirred at room temperature for 2 hours and treated with diisopropylamine (40 mL, 286 mmol) at 0.degree. C. After stirring at room temperature for overnight, the reaction is partitioned between ethyl acetate and 1N hydrochloride solution. The organic phase is washed with brine, dried over sodium sulfate, and concentrated in vacuo to afford 4-hydroxy-N,N-bis(1-methylethyl)benzamide.

Detailed Description Text (34):

A stirred solution of 4-hydroxy-N,N-bis(1-methylethyl)benzamide (2.47 g, 11.2 mmol) in 50 mL of N,N-dimethylformamide is treated with 60% sodium hydride (500 mg, 12.5 mmol). After stirring at 0.degree. C. for 10 minutes, the reaction is treated with 5-(4-cyanophenoxy)pentyl chloride (3.25 g, 14.5 mmol) and stirred at 70.degree. C. for 2 hours. The reaction is partitioned between ethyl acetate and water. The organic layer is washed with water and brine, dried over sodium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (60 g) with 70-80% ethyl acetate/hexane as the eluent to afford 4-[5-(4-cyanophenoxy)pentyloxy]N,N-bis(1-methylethyl)benzamide.

Detailed Description Text (41):

A stirred solution of 4-[4-(4-cyanophenoxy)butoxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide (500 mg, 1.18 mmol) in 2 mL of water and 8 mL of ethanol is treated with sodium hydroxide (57.7 mg, 1.34 mmol) and hydroxylamine hydrochloride (90 mg, 1.29 mmol). After refluxing overnight, the reaction is partitioned between dichloromethane and brine. The organic phase is dried over magnesium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (15 g) with ethyl acetate as the eluent to afford 4-[4-[4-[amino(hydroxyimino)methyl]phenoxy]butoxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide as colorless crystals, mp=63.degree.-65.degree. C.;

Detailed Description Text (43):

The starting material, 4-[4-(4-cyanophenoxy)butoxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide, can be prepared, for example, as follows:

Detailed Description Text (44):

A stirred solution of 4-hydroxy-3-methoxy-benzoic acid (5 g, 29.7 mmol) in 35 mL of dichloromethane is treated with thionyl chloride (20 mL, 377 mmol) and N,N-dimethylformamide (1.0 mL, 12.9 mmol). This solution is refluxed for 45 minutes and concentrated in vacuo. The resulting material is dissolved in 125 mL of dichloromethane and treated with diisopropylamine (20 mL, 143 mmol). After stirring at room temperature for 5 minutes, the reaction is diluted with ethyl acetate and

filtered. The filtrate is washed with 1N hydrochloride solution, and brine, dried over magnesium sulfate, and concentrated in vacuo to afford 4-hydroxy-3-methoxy-N,N-bis(1-methylethyl)benzamide as a colorless solid.

Detailed Description Text (45):

A stirred solution of 4-hydroxy-3-methoxy-N,N-bis(1-methylethyl)benzamide (1.0 g, 4.0 mmol) in 50 mL of N,N-dimethylformamide is treated with 60% sodium hydride (160 mg, 4.0 mmol). After stirring at 0.degree. C. for 10 minutes, the reaction is treated with 4-(4-cyanophenoxy)butyl chloride (835 mg, 4.0 mmol) and stirred at 60.degree. C. for 4 days. The reaction is partitioned between diethyl ether and water. The organic layer is washed with brine, dried over magnesium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (30 g) with 60 % ethyl acetate/hexane as the eluent to afford 4-[4-(4-cyanophenoxy)butoxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide as an oil.

Detailed Description Text (48):

(a) 4-[6-[4-[amino(hydroxyimino)methyl]phenoxy]hexyloxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide is obtained from 4-[6-(4-cyanophenoxy)hexyloxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide as a colorless foam;

Detailed Description Text (50):

(b) 4-[5-[4-[amino(hydroxyimino)methyl]phenoxy]pentyloxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide is obtained from 4-[5-(4-cyanophenoxy)pentyloxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide as colorless crystals, m.p.=56.degree.-58.degree. C.;

Detailed Description Text (52):

The starting material, 4-[5-(4-cyanophenoxy)pentyloxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide, can be prepared, for example, as follows:

Detailed Description Text (54):

A stirred solution of 4-[5-(4-cyanophenoxy)pentyloxy]-3-methoxy-N,N-bis(1-methylethyl)benzoic acid (7.24 g, 20.4 mmol) in 65 mL of dichloromethane is treated at 0.degree. C. with thionyl chloride (7.43 mL, 102 mmol) and N,N-dimethylformamide (7.2 mL, 93 mmol). This reaction mixture is refluxed overnight and concentrated in vacuo. The resulting material is dissolved with 100 mL of dichloromethane and treated with diisopropylamine (17 mL, 119 mmol). After stirring at room temperature for 4 hours, the reaction is concentrated in vacuo. The resulting material is partitioned between ethyl acetate and 1N hydrochloride solution. The organic phase is washed with brine, dried over magnesium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (300 g) with 60 % ethyl acetate/hexane as the eluent to afford 4-[5-(4-cyanophenoxy)pentyloxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide as a colorless solid.

Detailed Description Text (56):

A stirred solution of 4-[5-(4-cyano-3-fluoro-phenoxy)pentyloxy]-N,N-bis(1-methylethyl)benzamide (360 mg, 0.84 mmol) in 1.7 mL of 1N sodium hydroxide (1.7 mmol) and 10 mL of ethanol is treated with hydroxylamine hydrochloride (120 mg, 1.7 mmol). After refluxing overnight, the reaction is concentrated in vacuo. The resulting material is purified by chromatography on silica gel (500 g) with 60-70% ethyl acetate/hexane as the eluent to afford 4-[5-[4-[amino(hydroxyimino)methyl]-3-fluoro-phenoxy]pentyloxy]-N,N-bis(1-methylethyl)benzamide as a colorless foam;

Detailed Description Text (58):

The starting material, 4-[5-(4-cyano-3-fluoro-phenoxy)pentyloxy]-N,N-bis(1-methylethyl)benzamide, can be prepared, for example, as follows:

Detailed Description Text (61):

A stirred solution of 4-hydroxy-N,N-bis(1-methylethyl)benzamide (500 mg, 2.3 mmol) in 5 mL of N,N-dimethylformamide is treated with 1-bromo-5-chloropentane



(300 .mu.L, 2.3 mmol) and cesium carbonate (750 mg, 2.3 mmol) and heated for 2 hours. This is treated with a mixture of 2-fluoro-4-hydroxy-benzonitrile, and 60% sodium hydride (92 mg, 2.3 mmol) in 2 mL of N,N-dimethylformamide followed by sodium iodide (1.04 g, 6.9 mmol). The reaction is heated to 70.degree. C. for 6 hours and partitioned between ethyl acetate and water. The organic phase is washed with brine, dried over sodium sulfate, and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (20 g) with 70% ethyl acetate/hexane as the eluent to afford 4-[5-(4-cyano-3-fluoro-phenoxy)pentyl]oxy]-N,N-bis(1-methylethyl)benzamide.

Detailed Description Text (63):

A stirred solution of 4-[5-[4-[amino(hydroxyimino)methyl]phenoxy]pentyl]oxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide (200 mg, 0.4 mmol) in 4 mL of dichloromethane at 0.degree. C. is treated with aluminum chloride (292 mg, 2.2 mmol) and ethanethiol (4 mL, 54 mmol). After stirring at 0.degree. C. for 1 hour, reaction mixture is partitioned between ethyl acetate and saturated ammonium hydroxide solution. The organic phase is dried with magnesium sulfate and concentrated in vacuo. The resulting material is purified by chromatography on silica gel (10 g) with 5% methanol/dichloromethane as the eluent to afford 4-[5-[4-[amino(hydroxyimino)methyl]phenoxy]pentyl]oxy]-3-hydroxy-N,N-bis(1-methylethyl)benzamide as a colorless foam;

Detailed Description Paragraph Table (1):

	(1-methylethyl)benzamide
	Active ingredient 30.00 g Lactose 800.00 g
Avicel PH 102 300.00 g (microcrystalline cellulose)	Polyplasdone XL 30.00 g
(polyvinylpyrrolidone)	Purified water q.s Magnesium stearate 9.0 g

CLAIMS:

10. A compound according to claim 7 which is 4-[5-[4-[amino(hydroxyimino)methyl]-phenoxy]pentyl]oxy]-2-hydroxy-N,N-bis(1-methylethyl)benzamide, the compound of formula IB in which R.sub.1 is di-isopropylamino; R.sub.2 is hydroxy; X.sub.1 and X.sub.3 are O; X.sub.2 is pentylene; and R.sub.3 and R.sub.4 are hydrogen.

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L12: Entry 7 of 12

File: USPT

Aug 12, 1997

DOCUMENT-IDENTIFIER: US 5656293 A

TITLE: Delivery system for enhanced onset and increased potency

Detailed Description Text (7):

The composition may also contain a carbonate or bicarbonate to facilitate disintegration, or other such disintegrants. In addition, other excipients, useful in the art of tabletting, such as lubricants, binders, buffers, antioxidants, and colorants may be used. The tablet may be coated with a thin layer of a protective coating to provide a dustless and easily swallowed dosage form which is well known to those of skill in the art.

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L12: Entry 11 of 12

File: USPT

Feb 25, 1997

DOCUMENT-IDENTIFIER: US 5605889 A

TITLE: Method of administering azithromycin

Brief Summary Text (41):

In addition to the active ingredient azithromycin and a disintegrant, tablets according to this invention may be formulated to optionally include a variety of conventional excipients, depending on the exact formulation, such as binders, flavorings, buffers, diluents, colors, lubricants, sweetening agents, thickening agents, and glidants. Some excipients can serve multiple functions, for example as both binder and disintegrant.

Current US Cross Reference Classification (1):424/464

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L8






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### Search History

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L3: Entry 2 of 5

File: USPT

Mar 19, 1996

DOCUMENT-IDENTIFIER: US 5500422 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Benzamide derivative

Brief Summary Text (162):

The benzamide derivatives represented by formula (I) prepared according to the process described above and their pharmacologically acceptable salts have hyderfunctional activity on digestive tract and are useful for the treatment of gastrointestinal diseases. The compounds may preferably be formulated in a pharmaceutical composition as an active ingredient. The pharmaceutical composition comprising said compound as an active ingredient may generally be formulated and administered to a patient as orally available compositions such as, for example, capsules, tablets, subtilized granules, granules, powder or syrup, or administered as injection, suppository, eye drop, eye ointment, ear drop, or topical composition.

Brief Summary Text (163):

These pharmaceutical compositions can be prepared by ordinary methods. If necessary, pharmacologically and pharmaceutically acceptable additives may be added. For the preparation of orally available compositions and suppository, excipients such as, for example, lactose, D-mannitol, cornstarch, or crystalline cellulose; disintegrants such as, for example, carboxymethylcellulose or calcium carboxymethylcellulose; binders such as, for example, hydroxypropylcellulose, hydroxypropylmethylcellulose, or polyvinylpyrrolidone; lubricants such as, for example, magnesium stearate or talc; coating agents such as, for example, hydroxypropylmethylcellulose, sucrose, or titanium oxide; or bases such as, for example polyethylene glycol or hard fat may be used as pharmaceutical additives. For the preparation of an injection, eye drop, or ear drop, solubilizing agents or solubilizers such as, for example, distilled water for injection, saline, or propylene glycol which is useful for an aqueous composition or a composition for preparing aqueous solution before use; pH adjusting agents such as, for example, an inorganic or organic acid or base; isotonicity agents such as, for example, sodium chloride, glucose, or glycerin; or stabilizers may be used as pharmaceutical additives. For the preparation of eye ointment and topical composition, suitable pharmaceutical additives ordinarily formulated in ointment, cream, or cataplasms such as white vaseline, macrogol, glycerin, or cloth may be used.

Detailed Description Paragraph Table (1):

Formulation 1	Compound of Example 23	5 mg
Lactose	suitable amount	Cornstarch 15 mg
Magnesium Stearate	1 mg	80 mg
Formulation 2	Compound of Example 23	5 mg
Lactose	suitable amount	Cornstarch 15 mg
Magnesium Stearate	1 mg	Hydroxypropylmethylcellulose 4 mg
Polyethylene glycol	6000	0.5 mg
Titanium Oxide	0.5 mg	100 mg
Formulation 3	Compound of Example 23	10 mg
Lactose	suitable amount	<u>D-mannitol</u> 500 mg
Hydroxypropylcellulose	20 mg	Talc 2 mg
1,000 mg		
Formulation 4	Compound of Example 23	5 mg
Citric Acid	0.5 mg	Glucose 50 mg
Sodium Hydroxide	suitable amount	Distilled Water for Injection
suitable amount	1 ml	
Formulation 5	Compound of Example 23	5 mg
Hard Fat	1,295 mg	1,300 mg

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L3: Entry 3 of 5

File: USPT

Jan 30, 1996

DOCUMENT-IDENTIFIER: US 5488160 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Amidino compounds, their manufacture and method of treatment

Brief Summary Text (203):

The pharmacologically active compounds of the invention are useful in the manufacture of pharmaceutical compositions comprising an effective amount thereof in conjunction or admixture with excipients or carriers suitable for either enteral or parenteral application. Preferred are tablets and gelatin capsules comprising the active ingredient together with a) diluents, e.g. lactose, dextrose, sucrose, mannitol, sorbitol, cellulose and/or glycine; b) lubricants, e.g. silica, talcum, stearic acid, its magnesium or calcium salt and/or polyethyleneglycol; for tablets also c) binders e.g. magnesium aluminum silicate, starch paste, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose and or polyvinylpyrrolidone; if desired d) disintegrants, e.g. starches, agar, alginic acid or its sodium salt, or effervescent mixtures; and/or e) absorbants, colorants, flavors and sweeteners.

Brief Summary Text (204):

Injectable compositions are preferably aqueous isotonic solutions or suspensions, and suppositories are advantageously prepared from fatty emulsions or suspensions. Said compositions may be sterilized and/or contain adjuvants, such as preserving, stabilizing, wetting or emulsifying agents, solution promoters, salts for regulating the osmotic pressure and/or buffers. Cores of coated tablets are provided with suitable, optionally enteric, coatings, using, inter alia, concentrated sugar solutions which optionally contain gum arabic, talc, polyvinylpyrrolidone, polyethylene glycol and/or titanium dioxide, lacquer solutions in suitable organic solvents or solvent mixtures or, for the preparation of enteric coatings, solutions of suitable cellulose products such as acetyl cellulose phthalate or hydroxypropylmethylcellulose phthalate. Colorants or pigments can be added to the tablets or coatings of coated tablets, for example, to identify or to indicate various doses of active compound. In addition, they may also contain other therapeutically valuable substances. Said compositions are prepared according to conventional mixing, granulating or coating methods, respectively, and contain about 0.1 to 75%, preferably about 1 to 50%, of the active ingredient.

Detailed Description Text (205):

a) Preparation of 10,000 tablets each containing 20 mg of the active ingredient, for example, 4-[5-[4-(aminoiminomethyl)phenoxy]pentoxy]-3-methoxy-N,N-bis(1-methylethyl) benzamide (Z)-2-butenedioate (1:1):

Detailed Description Text (206):

Procedure: All the powders are passed through a screen with openings of 0.6 mm. The drug substance, lactose, magnesium stearate and haft of the starch are mixed in a suitable mixer. The other half of the starch is suspended in 65 ml of water and the suspension added to the boiling solution of the polyethylene glycol in 250 ml of water. The paste formed is added to the powders, which are granulated, if necessary, with an additional amount of water. The granulate is dried overnight at 35.degree. C. broken on a screen with 1.2 mm openings and compressed into tablets,

using concave punches uppers bisected.

Detailed Description Text (209):

Procedure: All the powders are passed through a screen with openings of 0.6 mm. The drug substance is placed in a suitable mixer and mixed first with the magnesium stearate, then with the lactose and starch until homogenous. No. 2 hard gelatin capsules are filled with 300 mg of said mixture each, using a capsule filling machine.

Detailed Description Paragraph Table (1):

	active ingredient	200.00 g	Lactose	2,535.00
g Corn <u>starch</u>	125.00 g	Polyethylene glycol 6,000	150.00 g	Magnesium stearate 40.00
g Purified water	q.s.			

Detailed Description Paragraph Table (2):

	active ingredient	40.00 g	Lactose	177.00 g
Modified <u>starch</u>	80.00 g	Magnesium stearate	3.00 g	

Detailed Description Paragraph Table (3):

	Active ingredient	75.00 g	Lactose	750.00 g
Avicel PH 102	300.00 g (microcrystalline <u>cellulose</u> )	Polyplasdone XL	30.00 g	
(polyvinylpyrrolidone)	Purified water	q.s.	Magnesium stearate	9.0 g

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☐ 1. Document ID: US 6365185 B1

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L3: Entry 1 of 5

File: USPT

Apr 2, 2002

US-PAT-NO: 6365185

DOCUMENT-IDENTIFIER: US 6365185 B1

\*\* See image for Certificate of Correction \*\*

TITLE: Self-destructing, controlled release peroral drug delivery system

DATE-ISSUED: April 2, 2002

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ritschel; Wolfgang A.	Cincinnati	OH		
Agrawal; Mukul A.	Strongsville	OH		

US-CL-CURRENT: 424/473; 424/464, 424/465, 424/466, 424/468, 424/469, 424/470,  
424/471, 424/472

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	INNO	Drawings
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☐ 2. Document ID: US 5500422 A

L3: Entry 2 of 5

File: USPT

Mar 19, 1996

US-PAT-NO: 5500422

DOCUMENT-IDENTIFIER: US 5500422 A

\*\* See image for Certificate of Correction \*\*

TITLE: Benzamide derivative

DATE-ISSUED: March 19, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ito; Yasuo	Katsuyama			JP
Kato; Hideo	Fukui			JP
Yasuda; Shingo	Katsuyama			JP
Iwasaki; Nobuhiko	Katsuyama			JP
Nishino; Hiroyuki	Katsuyama			JP

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US-CL-CURRENT: 514/211.09; 514/214.03, 514/227.5, 514/238.8, 514/331, 514/428,  
540/610, 544/169, 544/58.4, 546/221, 546/233, 548/146, 548/215, 548/557, 548/567

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 3. Document ID: US 5488160 A

L3: Entry 3 of 5

File: USPT

Jan 30, 1996

US-PAT-NO: 5488160

DOCUMENT-IDENTIFIER: US 5488160 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Amidino compounds, their manufacture and method of treatment

DATE-ISSUED: January 30, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Morrissey; Michael M.	Danville	CA		

US-CL-CURRENT: 564/165; 544/162, 546/226, 546/316, 546/323, 560/27, 564/157,  
564/47, 564/48, 564/91, 564/99

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 4. Document ID: US 5451700 A

L3: Entry 4 of 5

File: USPT

Sep 19, 1995

US-PAT-NO: 5451700

DOCUMENT-IDENTIFIER: US 5451700 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Amidino compounds, their manufacture and methods of treatment

DATE-ISSUED: September 19, 1995

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Morrissey; Michael M.	Danville	CA		
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US-CL-CURRENT: 564/165; 546/226, 560/27, 564/157, 564/47, 564/48, 564/91, 564/99

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 5. Document ID: US 5395832 A

L3: Entry 5 of 5

File: USPT

Mar 7, 1995

US-PAT-NO: 5395832

DOCUMENT-IDENTIFIER: US 5395832 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Benzamide derivatives

DATE-ISSUED: March 7, 1995

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ito; Yasuo	Katsuyama			JP
Kato; Hideo	Fukui			JP
Yasuda; Shingo	Katsuyama			JP
Iwasaki; Nobuhiko	Katsuyama			JP
Nishino; Hiroyuki	Katsuyama			JP
Takeshita; Makoto	Katsuyama			JP

US-CL-CURRENT: 514/210.16, 514/211.09, 514/214.03, 514/299, 514/304, 514/413,  
540/585, 546/112, 546/124, 546/130, 546/183, 548/452

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	DOC	Drawings
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L6: Entry 2 of 2

File: USPT

Apr 2, 2002

DOCUMENT-IDENTIFIER: US 6365185 B1

**\*\* See image for [Certificate of Correction](#) \*\***

TITLE: Self-destructing, controlled release peroral drug delivery system

Detailed Description Text (45):

Wall section 12 preferably comprises a composition comprising means that aids in controlling fluid flux into the compartment area occupied by the expandable driving member (also referred to as a push means). The composition is permeable to the passage of external fluids such as water and biological fluids, and it is substantially impermeable to the passage of beneficial agents, osmopolymers, osmagents, and the like. Typical compositions comprising semipermeable materials for forming wall 12 are, in one presently preferred embodiment, a member selected from the group consisting of a cellulose ester, a cellulose ether and a cellulose ester-ether. These cellulosic polymers have a degree of substitution, D.S., on the anhydroglucose unit, from greater than 0 up to 3 inclusive. By, "degree of substitution," or "D.S.," is meant the average number of hydroxyl groups originally present on the anhydroglucose unit comprising the cellulose polymer that are replaced by a substituting group. Representative materials include, but are not limited to, a member selected from the group consisting of cellulose acylate, cellulose diacylate, cellulose triacylate, cellulose acetate, cellulose diacetate, cellulose triacetate, mono-, di-, and tricellulose alkanylates, mono-, di-, and tricellulose aroylates, and the like. Exemplary cellulosic polymers include cellulose acetate having a D.S. up to 1 and an acetyl content up to 21% by molecular weight; cellulose acetate having a D.S. of 1 to 2 and an acetyl content of 21% to 35%; cellulose acetate having a D.S. of 2 to 3 and an acetyl content of 35% to 44.8%, and the like. More specific cellulosic polymers include cellulose propionate having a D.S. of 1.8 and a propionyl content of 39.2% to 45% and a hydroxyl content of 2.8% to 5.4%; cellulose acetate butyrate having a D.S. of 1.8 and an acetyl content of 13% to 15% and a butyryl content of 34% to 39%; cellulose acetate butyrate having an acetyl content of 2% to 29%, a butyryl content of 17% to 53% and a hydroxyl content of 0.5% to 4.7%; cellulose acetate butyrate having a D.S. of 1.8, and acetyl content of 4% average weight percent and a butyryl content of 51%; cellulose triacylates having a D.S. of 2.9 to 3 such as cellulose trivalerate, cellulose trilaurate, cellulose tripalmitate, cellulose trisuccinate, and cellulose trioctanoate; cellulose diacylates having a D.S. of 2.2 to 2.6 such as cellulose disuccinate, cellulose dipalmitate, cellulose dioctanoate, cellulose dipentate; coesters of cellulose such as cellulose acetate butyrate and cellulose, cellulose acetate propionate, and the like. The amount of semipermeable materials presently preferred in the shell is about 20% to 100%.

Detailed Description Text (50):

The matrix comprises a material which can form films or coatings and typically comprises any of the porous membrane materials known in the tableting art. Typical materials for forming the membranes are those known in the art to form osmosis or reverse osmosis membranes, including polycation-polyanion membranes. The porous membrane materials include, but are not limited to, cellulose acetate, ethylcellulose, polymethacrylic acid esters and acrylic acid ester/methacrylic acid copolymer with quarternary ammonium groups, cellulose triacetate, agar acetate,

amylose triacetate, beta glucan acetate, beta glucan triacetate, cellulose acetate ethyl carbamate, cellulose acetate phthalate, cellulose acetate methyl carbamate, cellulose acetate succinate, cellulose acetate dimethylaminoacetate, cellulose acetate ethyl carbonate, cellulose acetate methyl sulfonate, cellulose acetate butyl sulfonate, cellulose ethers, cellulose acetate propionate, polyvinyl methyl ether polymers, cellulose acetate laurate, methyl cellulose, cellulose acetate p-toluene sulfonate, triacetate of locust bean gum, cellulose acetate with acetylated hydroxyethyl cellulose, hydroxylated ethylenevinylacetate, polymeric epoxides, alkylene oxide-alkyl glycidyl ethers, polyurethanes, and polyglycolic acid. Preferably, the membrane material is cellulose acetate, ethylcellulose, polymethacrylic acid esters and acrylic acid ester/methacrylic acid copolymer with quarternary ammonium groups.

Detailed Description Text (51):

Alternatively, the matrix of the self-destructing shell/membrane may be comprised of non-porous membrane materials in which pores have been formed. Typically, this is accomplished by including a water soluble pore-forming material in the insoluble, non-porous membrane material solution. When the membrane is exposed to an aqueous environment, the pore-forming material dissolves, resulting in the formation of pores. Thus, the porosity of the membrane is directly proportional to the amount of pore-forming material incorporated into the membrane. The non-porous membrane materials include, but are not limited to, acrylics, polyurethanes, silicones, polyethylenes, polyvinyl chlorides, and ethylcellulose. The pore-forming materials include, but are not limited to, lactose, sucrose, mannitol, polyethylene glycol (PEG), hydroxypropylmethylcellulose (HPMC) and surfactants or other soluble additives.

Detailed Description Text (53):

As shown in FIGS. 3-5, the disintegrant is typically a coated sphere 32. It is important that the disintegrant 32 include significant amounts of insoluble, swellable material in a core 34 which cannot be easily expressed (i.e., expelled) through the membrane 30. This aids in causing excessive hydrostatic pressure within the matrix 31 and the rupturing of the semi-permeable membrane, thus allowing massive drug release to occur. For example, insoluble polysaccharides like starch and cellulose which have high water swelling capabilities are preferred, but soluble hydrogels, such as polyethylene glycol, hydroxypropyl methylcellulose and hydroxyethyl cellulose, can be used.

Detailed Description Text (55):

The delay jacket typically comprises a binder, an osmotic agent, and a tablet lubricant. Suitable binders include, but are not limited to, acacia, alginic acid, carboxymethylcellulose sodium, dextrin, ethylcellulose, gelatin, glucose, guar gum, hydroxyethyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl magnesium aluminum silicate, methylcellulose, microcrystalline cellulose, polyethylene oxide, polymethyl methacrylates, polyvinylpyrrolidone, pregelatinized starch, sodium alginate, syrup, and zein. Suitable osmotic agents include, but are not limited to, inorganic salts such as sodium, potassium or magnesium chloride, or sodium or potassium hydrogen or dihydrogen phosphate; salts of organic acids such as sodium alginate, sodium ascorbate, sodium benzoate, sodium citrate, edetate disodium, sodium fumarate, sodium or potassium acetate, or magnesium succinate; organic acids such as alginic acid, ascorbic acid, citric acid, edetic acid, malic acid, or sorbic acid; carbohydrates such as dextrates, sorbitol, xylitol, maltitol, mannitol, arabinose, ribose, xylose, glucose, dextrose, fructose, galactose, mannose, sucrose, maltose, lactose, or raffinose; water-soluble amino acids such as glycine, leucine, alanine or methionine; or miscellaneous others such as magnesium sulfate, magnesium carbonate, urea, saccharin, sodium saccharin, glycerin, hexylene glycol, polyethylene glycol, or propylene glycol; and mixtures thereof. Suitable tablet lubricants include, but are not limited to, calcium stearate, glyceryl behenate, hydrogenated vegetable oils, magnesium stearate, mineral oil, polyethylene glycol, sodium stearyl fumarate, stearic acid, talc, and zinc

stearate.

Detailed Description Text (59):

The semi-permeable membrane containing the disintegrant embedded in the matrix may be applied using conventional coating techniques known in the art, for example fluidized bed spraying and compression coating. The choice of semi-permeable membrane plays an important role in controlling the release of the active agent. For example, it is known that the acetyl value is an important factor in determining the release rate from membranes constructed from cellulose acetate. Compendial grade cellulose acetate is commercially available with nominal acetyl values of either 32% or 40% by weight. Membranes constructed from material at 32% by weight acetyl value release drug from similar drug cores at a faster rate than do membranes constructed with the same amount of cellulose acetate by weight having a 40% acetyl value.

Detailed Description Text (62):

The delay jacket typically comprises a binder, an osmotic agent, and a tablet lubricant. Suitable binders include, but are not limited to, acacia, alginic acid, carboxymethylcellulose sodium, dextrin, ethylcellulose, gelatin, glucose, guar gum, hydroxyethyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl magnesium aluminum silicate, methylcellulose, microcrystalline cellulose, polyethylene oxide, polymethylmethacrylates, polyvinylpyrrolidone, pregelatinized starch, sodium alginate, syrup, and zein. Suitable osmotic agents include, but are not limited to, inorganic salts such as sodium, potassium or magnesium chloride, or sodium or potassium hydrogen or dihydrogen phosphate; salts of organic acids such as sodium alginate, sodium ascorbate, sodium benzoate, sodium citrate, edetate disodium, sodium fumarate, sodium or potassium acetate, or magnesium succinate; organic acids such as alginic acid, ascorbic acid, citric acid, edetic acid, malic acid, or sorbic acid; carbohydrates such as dextrates, sorbitol, xylitol, maltitol, mannitol, arabinose, ribose, xylose, glucose, dextrose, fructose, galactose, mannose, sucrose, maltose, lactose, or raffinose; water-soluble amino acids such as glycine, leucine, alanine or methionine; or miscellaneous others such as magnesium sulfate, magnesium carbonate, urea, saccharin, sodium saccharin, glycerin, hexylene glycol, polyethylene glycol, or propylene glycol; and mixtures thereof. Suitable tablet lubricants include, but are not limited to, calcium stearate, glyceryl behenate, hydrogenated vegetable oils, magnesium stearate, mineral oil, polyethylene glycol, sodium stearyl fumarate, stearic acid, talc, and zinc stearate.

Detailed Description Text (68):

The expandable push means 50 operable for pushing the beneficial agent composition 23 from delivery system 10, comprises, in a presently preferred embodiment, a swellable hydrophilic polymer. Hydrophilic polymers are known also as osmopolymers. The push means 50 interacts with water and aqueous biological fluids and swells or expands. Osmopolymers exhibit the ability to swell in water and to retain a significant portion of the imbibed and absorbed water within the polymer structure. The osmopolymers swell or expand to a very high degree, usually exhibiting a 2 to 50 fold volume increase. The osmopolymers can be noncross-linked or cross-linked. The swellable, hydrophilic polymers are, in one presently preferred embodiment, lightly cross-linked, such as cross-links being formed by covalent or ionic bonds. The osmopolymers can be of plant, animal or synthetic origin. Hydrophilic polymers suitable for the present purpose include poly(hydroxyalkylmethacrylate) having a molecular weight of from 30,000 to 5,000,000; poly(vinylpyrrolidone) having molecular weight of from 10,000 to 360,000; anionic and cationic hydrogels; polyelectrolyte complexes; poly(vinyl alcohol) having a low acetate residual, cross-linked with glyoxal, formaldehyde, or glutaraldehyde and having a degree of polymerization from 200 to 30,000; a mixture of methyl cellulose, cross-linked agar and carboxymethyl cellulose; a water insoluble, water swellable copolymer produced by forming a dispersion of finely divided copolymer of maleic anhydride with styrene, ethylene, propylene, butylene or isobutylene cross-linked with from 0.0001

to about 0.5 moles of polyunsaturated cross-linking agent per mole of maleic anhydride in the copolymer; water swellable polymers of N-vinyl lactams, and the like.

Detailed Description Text (69):

Other osmopolymers operable as the expandable driving member 50 (also referred to as the push means) and initially surrounded by wall section 12 comprise polymers that form hydrogels such as Carbopol.RTM. acidic carboxy polymers generally having a molecular weight of 450,000 to 4,000,000; the sodium salt of Carbopol.RTM. acidic carboxy polymers and other metal salts; Cyanamer.RTM. polyacrylamides; cross-linked water swellable indine-maleic anhydride polymers; Goodrite.RTM. polyacrylic acid having, but not limited to, a molecular weight of 80,000 to 200,000, and the sodium and other metal salts; Polyox.RTM. polyethylene oxide polymers having a molecular weight of 100,000 to 5,000,000; starch graft copolymers; AquaKeeps.RTM. acrylate polymers; diester cross-linked linked polyglucan, and the like. Representative polymers that form hydrogels are known to the prior art in U.S. Pat. No. 3,865,108 issued to Hartop; U.S. Pat. No. 4,002,173 issued to Manning; U.S. Pat. No. 4,207,893 issued to Michaels, and in Handbook of Common Polymers, by Scott and Roff, published by the Chemical Rubber Company, CRC Press, Cleveland, Ohio, the disclosure of each of these publications being incorporated herein in its entirety by reference.

Detailed Description Text (72):

The expandable push means 50 in another preferred embodiment comprises an optional osmagent 26 dispersed therein. The osmagents are known also as osmotically effective solutes and they are also known as osmotically effective compounds. The osmotically effective compounds that can be used for the purpose of this invention include inorganic and organic compounds that exhibit an osmotic pressure gradient across a semipermeable wall. The osmotically effective compounds, along with the osmopolymers, imbibe fluid into the device thereby making available in situ fluid for imbibition by an osmopolymer to enhance its expansion. The osmotically effective compounds are used by mixing them with the osmopolymer, homogeneously or heterogeneously and then charging them into the delivery system. Osmotically effective solutes used for the former purpose include magnesium sulfate, magnesium chloride, sodium chloride, potassium chloride, potassium sulfate, sodium sulfate, lithium sulfate, potassium acid phosphate, d-mannitol, urea, inositol, magnesium succinate, tartaric acid, carbohydrates such as raffinose, sucrose, glucose, alpha - d-lactose monohydrate, mannitol, and mixtures thereof. The amount of osmagent in the blend with the osmopolymer usually is from 1% to 40%, or higher, with the total of all ingredients comprising the second composition equal to 100%.

Detailed Description Text (73):

The expandable push means 50 in another preferred embodiment comprises an osmagent. The osmagent can comprise a tablet, a layer, or osmagent can be pressed into wall section 12. The osmagent can be in any suitable form such as particles, crystals, pellets, granules, and the like, when pressed into a tablet layer and into wall section 12. Various osmotically effective solutes comprising magnesium sulfate, magnesium chloride, sodium chloride, lithium chloride, potassium sulfate, sodium carbonate, sodium sulfite, lithium sulfate, potassium chloride, calcium carbonate, potassium acid phosphate, sodium lactate, calcium lactate, mannitol, urea, inositol, magnesium succinate, tartaric acid, soluble carbohydrates such as raffinose, sucrose, glucose, lactose, mixtures thereof, and the like, can be used for this embodiment. The osmotic pressure of an osmagent, or an osmopolymer, can be measured using an osmometer. An osmometer used for the present measurements is identified as Model 320B, Vapor Pressure Osmometer, manufactured by the Hewlett Packard Co., Avondale, Pa. Osmagents and osmopolymers are known to the art in U.S. Pat. Nos. 4,327,725 and 4,612,008, the disclosure of each of these patents being incorporated herein in its entirety by reference.

Detailed Description Text (74):

Other gelable, fluid imbibing and retaining polymers useful for forming the hydrophilic, expandable push means 50 include pectin having a molecular weight ranging from 30,000 to 300,000; polysaccharides such as agar, acacia, karaya, traga anth, algin and guar; Carbopol.RTM. acidic carboxy polymer and its salt derivatives; polyacrylamides; water-swellaable indene maleic anhydride polymers; Good-rite.RTM. polyacrylic acid having a molecular weight of 80,000 to 200,000; Polyox.RTM. polyethylene oxide polymers having a molecular weight of 100,000 to 7,500,000; starch graft copolymers; Aqua-Keep.RTM. acrylate polymers with water absorbability of about 400 times its original weight; diesters of polyglucan; a mixture of cross-linked polyvinyl alcohol and poly(N-vinyl-2-pyrrolidone); zein available as prolamine; poly(ethylene glycol) having a molecular weight of 4,000 to 100,000; and the like. In a preferred embodiment, the expandable member is formed from polymers and polymeric compositions that are thermoformable. Representative polymers possessing hydrophilic properties are known in U.S. Pat Nos. 3,865,108; 4,002,173; 4,207,893; 4,327,725, and in Handbook of Common Polymers; by Roff and Scott, published by Cleveland Rubber Company, Cleveland, Ohio, the disclosure of each of these documents being incorporated herein in its entirety by reference.

Detailed Description Text (77):

Examples of such water-soluble compounds for inducing osmosis in the core include inorganic salts such as sodium, potassium or magnesium chloride, or sodium or potassium hydrogen or dihydrogen phosphate; salts of organic acids such as sodium alginate, sodium ascorbate, sodium benzoate, sodium citrate, edetate disodium, sodium fumarate, sodium or potassium acetate, or magnesium succinate; organic acids such as alginic acid, ascorbic acid, citric acid, edetic acid, malic acid, or sorbic acid; carbohydrates such as dextrates, sorbitol, xylitol, maltitol, mannitol, arabinose, ribose, xylose, glucose, dextrose, fructose, galactose, mannose, sucrose, maltose, lactose, or raffinose; water-soluble amino acids such as glycine, leucine, alanine or methionine; or miscellaneous others such as magnesium sulfate, magnesium carbonate, urea, saccharin, sodium saccharin, glycerin, hexylene glycol, polyethylene glycol, or propylene glycol; and mixtures thereof.

Detailed Description Text (79):

Additional core excipients may include tableting lubricants, glidants, wetting agents to aid in dissolution of the components, binders, and suspending/thickening agents. Suitable lubricants include, but are not limited to, calcium stearate, glyceryl behenate, hydrogenated vegetable oils, magnesium stearate, mineral oil, polyethylene glycol, sodium stearyl fumarate, stearic acid, talc, and zinc stearate. Suitable glidants include, but are not limited to, fused or colloidal silicon dioxide, calcium silicate, magnesium silicate, talc, and silica hydrogel. Suitable wetting agents include, but are not limited to, benzalkonium chloride, benzethonium chloride, cetylpyridinium chloride, docusate sodium, lecithin, nonoxynol 9, nonoxynol 10, octoxynol 9, poloxamer, polyoxyl 35 castor oil, polyoxyl 40 hydrogenated castor oil, polyoxyl 50 stearate, polyoxyl 10 oleyl ether, polyoxyl 20 cetostearyl ether, polyoxyl 40 stearate, polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80, sodium lauryl surfate, sorbitan esters, polyoxyethylene sorbitan fatty acid esters, and Tyloxapol (4-(1,1,3,3-tetramethylbutyl)phenol polymer with formaldehyde and oxirane). Suitable binders include, but are not limited to, acacia, alginic acid, carboxymethylcellulose sodium, dextrin, ethylcellulose, gelatin, glucose, guar gum, hydroxyethyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl magnesium aluminum silicate, methylcellulose, microcrystalline cellulose, polyethylene oxide, polymethylmethacrylates, polyvinylpyrrolidone, pregelatinized starch, sodium alginate, syrup, and zein. Suitable suspending/thickening agents include acacia, agar, alginic acid, bentonite, carbomer, carboxymethylcellulose calcium, carageenan, carboxymethylcellulose sodium, corn starch, dextrin, gelatin, guar gum, hydroxyethyl cellulose, hydroxypropyl cellulose, hydroxypropyl methylcellulose, kaolin, lecithin, magnesium aluminum silicate, methylcellulose, microcrystalline cellulose, pectin, poloxamer, polyethylene glycol alginate, polyethylene oxide, polyvinyl alcohol, polyvinylpyrrolidone, vinyl acetate, powdered cellulose,



pregelatinized starch, propylene glycol alginate, silicon dioxide, sodium alginate, tragacanth, and xanthan gum.

Detailed Description Text (88):

An enteric delay jacket coating 40 may be included to prevent the dissolution of the jacket and core in the stomach. It may consist of any pharmaceutically acceptable material which is gastric fluid resistant, that is a material soluble only in fluids with a pH greater than that of the stomach. Enteric coating materials include, but are not limited to, cellulose acetate phthalate NF, hydroxypropyl methylcellulose phthalate NF, polyvinyl acetate phthalate NF, and methacrylic acid copolymer NF. Thus, in a low pH environment, the enteric coating will be insoluble and hinder intrusion of water through the semi-permeable membrane which could otherwise dissolve the delay jacket. It may be applied over the semi-permeable membrane using conventional film coating techniques known in the art, for example perforated pan coating.

CLAIMS:

6. The tablet of claim 5 wherein the insoluble polysaccharide is selected from the group consisting of starch, cellulose, and combinations thereof.

7. The tablet of claim 5 wherein the hydrogel is selected from the group consisting of polyethylene glycol, hydroxypropyl methylcellulose, hydroxyethyl cellulose, and combinations thereof.

8. The tablet of claim 5 wherein the swellable, hydrophilic polymer is selected from the group consisting of poly(hydroxyalkylmethacrylate, poly(vinylpyrrolidone, polyelectrolyte complexes, poly(vinyl alcohol, methyl cellulose, cross-linked agar, carboxymethyl cellulose, and combinations thereof.

10. The tablet of claim 5 wherein the polymer which forms a hydrogel upon contact with an imbibed fluid is selected from the group consisting of an acidic carboxy polymer, a metal salt of an acidic carboxy polymer, a polyacrylamide, a cross-linked, water-swellable, indine-maleic anhydride polymer, a polyacrylic acid, a metal salt of a polyacrylic acid, a polyethylene oxide polymer, a starch graft copolymer, an acrylate polymer; a diester cross-linked polyglucan, and combinations thereof.

12. The tablet of claim 3 wherein the matrix includes a material selected from the group consisting of cellulose acetate, ethylcellulose, a polymethacrylic acid ester, an acrylic acid ester/methacrylic acid copolymer with at least one quarternary ammonium group, cellulose triacetate, agar acetate, amylose triacetate, beta glucan acetate, beta glucan triacetate, cellulose acetate ethyl carbamate, cellulose acetate phthalate, cellulose acetate methyl carbamate, cellulose acetate succinate, cellulose acetate dimethylaminoacetate, cellulose acetate ethyl carbonate, cellulose acetate methyl sulfonate, cellulose acetate butyl sulfonate, a cellulose ether, cellulose acetate propionate, a polyvinyl methyl ether polymer, cellulose acetate laurate, methyl cellulose, cellulose acetate p-toluene sulfonate, triacetate of locust bean gum, cellulose acetate with acetylated hydroxyethyl cellulose, hydroxylated ethylenevinylacetate, a polymeric epoxide, an alkylene oxide-alkyl glycidyl ether, a polyurethane, polyglycolic acid, and combinations thereof.

13. The tablet of claim 3 wherein the matrix includes a material selected from the group consisting of cellulose acetate, ethylcellulose, a polymethacrylic acid ester, an acrylic acid ester/methacrylic acid copolymer with at least one quarternary ammonium group, and combinations thereof.

15. The tablet of claim 14 wherein the aqueously dispersible, pharmaceutically acceptable, polymeric compound is selected from the group consisting of a

methacrylic ester copolymer, poly(ethyl acrylate, methyl methacrylate), poly(ethyl acrylate, methyl methacrylate, trimethylammonioethyl methacrylate chloride), a polymethyl methacrylate-methacrylic acid copolymer, cellulose acetate, ethylcellulose, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, and combinations thereof.

19. The tablet of claim 1 wherein the first beneficial agent is selected from the group consisting of theophylline, IGF-1, PTH (1-34), TGF alpha, TGF beta 1, TGF beta 2, TGF beta 3, IFN alpha, hybrid IFN alpha, IFN gamma, hirudin, heparin, calcitonin, 5-aminosalicylic acid, N-hydroxy-N-((6-phenoxy-2H-1-benzopyran-3-yl) methyl)-urea, 4-[5-[4-(aminoiminomethyl)phenoxy]pentoxy]-3-methoxy-N,N-bis(1-methylethyl)benzamide (Z)-2-butenedioate, N-[2-[[2-[[4-(4-fluorophenyl)phenyl] methyl]-1,2,3,4-tetrahydro-1-oxo-6-iso quinolinyl]oxy]ethyl]-N-hydroxyurea, 1-(1-benzo[b]thien-2-ylethyl)-1-hydroxyurea, 5-[2-(2-carboxyethyl)-3-[6-(para-methoxyphenyl)-5E-hexenyl]oxyphenoxy]valeric acid, beclomethasone dipropionate, betamethasone-17-valerate, prednisolone metasulfobenzoate, tixocortol pivalate, budesonide, fluticasone, metoprolol, a pharmaceutically acceptable salt thereof, and combinations thereof.

24. The tablet of claim 23 wherein the enteric coating is selected from the group consisting of cellulose acetate phthalate NF, hydroxypropyl methylcellulose phthalate NF, polyvinyl acetate phthalate NF, methacrylic acid copolymer NF, and combinations thereof.

33. The tablet of claim 32 wherein the insoluble polysaccharide is selected from the group consisting of starch, cellulose, and combinations thereof.

34. The tablet of claim 32 wherein the hydrogel is selected from the group consisting of polyethylene glycol, hydroxypropyl methylcellulose, hydroxyethyl cellulose, and combinations thereof.

35. The tablet of claim 32 wherein the swellable, hydrophilic polymer is selected from the group consisting of poly(hydroxyalkylmethacrylate), poly(vinylpyrrolidone), polyelectrolyte complexes, poly(vinyl alcohol), methyl cellulose, cross-linked agar, carboxymethyl cellulose, and combinations thereof.

37. The tablet of claim 32 wherein the polymer which forms a hydrogel upon contact with an imbibed fluid is selected from the group consisting of an acidic carboxy polymer, a metal salt of an acidic carboxy polymer, a polyacrylamide, a cross-linked, water-swellable, indine-maleic anhydride polymer, a polyacrylic acid, a metal salt of a polyacrylic acid, a polyethylene oxide polymer, a starch graft copolymer, an acrylate polymer; a diester cross-linked polyglucan, and combinations thereof.

44. The tablet of claim 40 wherein the carbohydrate is selected from the group consisting of a dextrate, sorbitol, xylitol, maltitol, mannitol, arabinose, ribose, xylose, glucose, dextrose, fructose, galactose, mannose, sucrose, maltose, lactose, raffinose, and combinations thereof.

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☐ 1. Document ID: US 6949259 B1

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L6: Entry 1 of 2

File: USPT

Sep 27, 2005

US-PAT-NO: 6949259

DOCUMENT-IDENTIFIER: US 6949259 B1

TITLE: Solid preparations for oral use

DATE-ISSUED: September 27, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ohyama; Toshinori	Nogi-machi			JP
Imamizu; Masaru	Nogi-machi			JP

US-CL-CURRENT: [424/474](#); [424/464](#), [424/465](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Index	Drawings
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☐ 2. Document ID: US 6365185 B1

L6: Entry 2 of 2

File: USPT

Apr 2, 2002

US-PAT-NO: 6365185

DOCUMENT-IDENTIFIER: US 6365185 B1

**\*\* See image for [Certificate of Correction](#) \*\***

TITLE: Self-destructing, controlled release peroral drug delivery system

DATE-ISSUED: April 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ritschel; Wolfgang A.	Cincinnati	OH		
Agrawal; Mukul A.	Strongsville	OH		

US-CL-CURRENT: [424/473](#); [424/464](#), [424/465](#), [424/466](#), [424/468](#), [424/469](#), [424/470](#), [424/471](#), [424/472](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	Index	Drawings
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L7: Entry 3 of 9

File: USPT

Mar 19, 1996

DOCUMENT-IDENTIFIER: US 5500422 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Benzamide derivative

Brief Summary Text (15):

Examples of pharmacologically acceptable salts of the benzamide derivatives of the present invention include alkali-addition salts or acid-addition salts. Examples of the alkali-addition salts include, for example, inorganic alkali-addition salts such as, for example, sodium salt, potassium salt, calcium salt, and ammonium salt, and organic base-addition salts such as, for example, ethylenediamine salt, ethanolamine salt, N,N-dialkylethanolamine salt, and triethanolamine salt. Examples of the acid addition salts include, for example, inorganic acid-addition salts such as, for example, hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate, and phosphate, and organic acid-addition salts such as, for example, acetate, maleate, fumarate, citrate, oxalate, tartrate, malate, mandelate, methanesulfonate, p-toluenesulfonate, and 10-camphorsulfonate.

Brief Summary Text (162):

The benzamide derivatives represented by formula (I) prepared according to the process described above and their pharmacologically acceptable salts have hyderfunctional activity on digestive tract and are useful for the treatment of gastrointestinal diseases. The compounds may preferably be formulated in a pharmaceutical composition as an active ingredient. The pharmaceutical composition comprising said compound as an active ingredient may generally be formulated and administered to a patient as orally available compositions such as, for example, capsules, tablets, subtilized granules, granules, powder or syrup, or administered as injection, suppository, eye drop, eye ointment, ear drop, or topical composition.

Brief Summary Text (163):

These pharmaceutical compositions can be prepared by ordinary methods. If necessary, pharmacologically and pharmaceutically acceptable additives may be added. For the preparation of orally available compositions and suppository, excipients such as, for example, lactose, D-mannitol, cornstarch, or crystalline cellulose; disintegrants such as, for example, carboxymethylcellulose or calcium carboxymethylcellulose; binders such as, for example, hydroxypropylcellulose, hydroxypropylmethylcellulose, or polyvinylpyrrolidone; lubricants such as, for example, magnesium stearate or talc; coating agents such as, for example, hydroxypropylmethylcellulose, sucrose, or titanium oxide; or bases such as, for example polyethylene glycol or hard fat may be used as pharmaceutical additives. For the preparation of an injection, eye drop, or ear drop, solubilizing agents or solubilizers such as, for example, distilled water for injection, saline, or propylene glycol which is useful for an aqueous composition or a composition for preparing aqueous solution before use; pH adjusting agents such as, for example, an inorganic or organic acid or base; isotonicity agents such as, for example, sodium chloride, glucose, or glycerin; or stabilizers may be used as pharmaceutical additives. For the preparation of eye ointment and topical composition, suitable pharmaceutical additives ordinarily formulated in ointment, cream, or cataplasms such as white vaseline, macrogol, glycerin, or cloth may be used.

Detailed Description Paragraph Table (1):

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Formulation 1 Compound of Example 23 5 mg Lactose suitable amount Cornstarch 15 mg Magnesium Stearate 1 mg 80 mg Formulation 2 Compound of Example 23 5 mg Lactose suitable amount Cornstarch 15 mg Magnesium Stearate 1 mg Hydroxypropylmethylcellulose 4 mg Polyethylene glycol 6000 0.5 mg Titanium Oxide 0.5 mg 100 mg Formulation 3 Compound of Example 23 10 mg Lactose suitable amount D-mannitol 500 mg Hydroxypropylcellulose 20 mg Talc 2 mg 1,000 mg Formulation 4 Compound of Example 23 5 mg Citric Acid 0.5 mg Glucose 50 mg Sodium Hydroxide suitable amount Distilled Water for Injection suitable amount 1 ml Formulation 5 Compound of Example 23 5 mg Hard Fat 1,295 mg 1,300 mg

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☐ 1. Document ID: US 6841565 B1

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L7: Entry 1 of 9

File: USPT

Jan 11, 2005

US-PAT-NO: 6841565

DOCUMENT-IDENTIFIER: US 6841565 B1

TITLE: Treatment of patients with chronic lymphocytic leukemia

DATE-ISSUED: January 11, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lucas; David M.	Hilliard	OH		
Parthun; Mark R.	Hilliard	OH		
Byrd; John C.	Columbus	OH		
Grever; Michael R.	Columbus	OH		

US-CL-CURRENT: [514/346](#); [514/352](#), [514/357](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 2. Document ID: US 6365185 B1

L7: Entry 2 of 9

File: USPT

Apr 2, 2002

US-PAT-NO: 6365185

DOCUMENT-IDENTIFIER: US 6365185 B1

\*\* See image for [Certificate of Correction](#) \*\*

TITLE: Self-destructing, controlled release peroral drug delivery system

DATE-ISSUED: April 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ritschel; Wolfgang A.	Cincinnati	OH		
Agrawal; Mukul A.	Strongsville	OH		

US-CL-CURRENT: [424/473](#); [424/464](#), [424/465](#), [424/466](#), [424/468](#), [424/469](#), [424/470](#), [424/471](#), [424/472](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 3. Document ID: US 5500422 A

L7: Entry 3 of 9

File: USPT

Mar 19, 1996

US-PAT-NO: 5500422

DOCUMENT-IDENTIFIER: US 5500422 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Benzamide derivative

DATE-ISSUED: March 19, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ito; Yasuo	Katsuyama			JP
Kato; Hideo	Fukui			JP
Yasuda; Shingo	Katsuyama			JP
Iwasaki; Nobuhiko	Katsuyama			JP
Nishino; Hiroyuki	Katsuyama			JP
Takeshita; Makoto	Katsuyama			JP

US-CL-CURRENT: 514/211.09; 514/214.03, 514/227.5, 514/238.8, 514/331, 514/428,  
540/610, 544/169, 544/58.4, 546/221, 546/233, 548/146, 548/215, 548/557, 548/567

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 4. Document ID: US 5488160 A

L7: Entry 4 of 9

File: USPT

Jan 30, 1996

US-PAT-NO: 5488160

DOCUMENT-IDENTIFIER: US 5488160 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Amidino compounds, their manufacture and method of treatment

DATE-ISSUED: January 30, 1996

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Morrissey; Michael M.	Danville	CA		

US-CL-CURRENT: 564/165; 544/162, 546/226, 546/316, 546/323, 560/27, 564/157,  
564/47, 564/48, 564/91, 564/99

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	FIGS	Drawings
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☐ 5. Document ID: US 5451700 A

L7: Entry 5 of 9

File: USPT

Sep 19, 1995

US-PAT-NO: 5451700

DOCUMENT-IDENTIFIER: US 5451700 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Amidino compounds, their manufacture and methods of treatment

DATE-ISSUED: September 19, 1995

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Morrissey; Michael M.	Danville	CA		
Suh; Hongsuk	Cedar Knolls	NJ		

US-CL-CURRENT: 564/165; 546/226, 560/27, 564/157, 564/47, 564/48, 564/91, 564/99

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 6. Document ID: US 5395832 A

L7: Entry 6 of 9

File: USPT

Mar 7, 1995

US-PAT-NO: 5395832

DOCUMENT-IDENTIFIER: US 5395832 A

**\*\* See image for Certificate of Correction \*\***

TITLE: Benzamide derivatives

DATE-ISSUED: March 7, 1995

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ito; Yasuo	Katsuyama			JP
Kato; Hideo	Fukui			JP
Yasuda; Shingo	Katsuyama			JP
Iwasaki; Nobuhiko	Katsuyama			JP
Nishino; Hiroyuki	Katsuyama			JP
Takeshita; Makoto	Katsuyama			JP

US-CL-CURRENT: 514/210.16; 514/211.09, 514/214.03, 514/299, 514/304, 514/413,  
540/585, 546/112, 546/124, 546/130, 546/183, 548/452

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 7. Document ID: US 5378728 A

L7: Entry 7 of 9

File: USPT

Jan 3, 1995

US-PAT-NO: 5378728

DOCUMENT-IDENTIFIER: US 5378728 A

TITLE: Benzoic acid derivatives as antidiabetic agents

DATE-ISSUED: January 3, 1995

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Nadelson; Jeffrey	Denville	NJ		
Simpson; William R. J.	Mendham	NJ		
Anderson; Robert C.	Andover	NJ		
Bajwa; Joginder S.	Stroudsburg	PA		

US-CL-CURRENT: 514/507; 514/544, 514/568, 514/621, 514/622, 560/51, 562/442,  
562/459, 564/155, 564/158, 564/169

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 8. Document ID: US 5064862 A

L7: Entry 8 of 9

File: USPT

Nov 12, 1991

US-PAT-NO: 5064862

DOCUMENT-IDENTIFIER: US 5064862 A

TITLE: Anticonvulsant method and formulations

DATE-ISSUED: November 12, 1991

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Clark; C. Randall	Auburn	AL		

US-CL-CURRENT: 514/617

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Drawings
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☐ 9. Document ID: US 4638014 A

L7: Entry 9 of 9

File: USPT

Jan 20, 1987

US-PAT-NO: 4638014

DOCUMENT-IDENTIFIER: US 4638014 A

TITLE: Anticonvulsant method and formulations

DATE-ISSUED: January 20, 1987

INVENTOR - INFORMATION :

NAME	CITY	STATE	ZIP CODE	COUNTRY
Clark; C. Randall	Auburn	AL		

US-CL-CURRENT: 514/619

Full	Title	Citation	Front	Review	Classification	Date	Reference			Claims	Index	Original
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